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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/653,182	08/31/2000	Paul D. Robbins	AP32573-A-A/072396.0203	4223

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EXAMINER
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TIZIO, STEVEN C

ART UNIT	PAPER NUMBER
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1627

DATE MAILED: 05/03/2002

13

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/653,182

Applicant(s)

ROBBINS ET AL.

Examiner

Steven C Tizio

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 12 March 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-59 is/are pending in the application.
- 4a) Of the above claim(s) 8-59 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-7 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 C
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

File  
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## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d):  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☒ Interview Summary (PTO-413) Paper No(s). 13
- 2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 8-9 6) ☐ Other:

**Detailed Action**

1. **Claims 1-59** are pending.
2. Applicant's election without traverse of Group I (**claims 1-7**) in Paper No. 12 is acknowledged.
3. Applicant's election without traverse of SEQ ID NO: 5 in Paper No. 12 is acknowledged.
4. The species elected (SEQ ID NO: 5) on 3/12/02, has been withdrawn, since the elected species is free of prior art.
5. **Claims 8-59** are withdrawn from consideration as not directed to the elected Group I.
6. **Claims 1- 7** are currently being examined.
7. The supplemental Information Disclosure Statement (IDS), filed on 4/16/01, has been acknowledged and considered on 4/15/02.

8. The second supplemental information disclosure statement, filed on 6/04/01, has been acknowledged and considered on 4/15/02.

9. This application has been filed with informal drawings. Applicant is invited to notice that the draftsman in PTO 948 checked boxes 3-6, 10, and 12. If applicant renumbers the figures, applicant is encouraged to amend the specification so that the description of renumbered figures corresponds to the renumbered figures.

10. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicants' cooperation is requested in correcting any errors of which applicant may become aware in the specification.

11. The disclosure is objected to because of the following informalities:

- 1) page 11, line 4: "histological ly" should be "histologically"
- 2) Page 23, line 8: "herpesvirus 1 probably" should be herpesvirus 1, which is probably a"
- 3) page 29, line 21: "in a" should be "in and"
- 4) page 60, lines 12 and 17: "histological ly" should be "histologically"

Appropriate correction is required.

12. Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "**said**," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

### **Claim Rejections - 35 USC § 112**

13. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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14. **Claims 1-7** are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for facilitating cellular internalization of a cargo and nuclear translocation using peptides SEQ ID NOS: 1-6, does not reasonably provide enablement for facilitating cellular internalization of a cargo and nuclear translocation using peptides of SEQ ID NOS: 7-18 and SEQ ID NOS: 25-75. According to the specification, the peptides of SEQ ID NOS: 1-6 are internalizing peptides, which is commensurate with the scope of the invention:

- 1) SEQ ID NOS: 2-5 facilitate the internalization of phage as well as the facilitation of the internalization of a cargo;
- 2) SEQ ID NOS: 3 and 5 facilitate the uptake of M13 phage labeled with Cy3;
- 3) SEQ ID NO: 5 facilitates the efficient internalization of the streptavidin-408 complex with a significant percentage of the peptide-streptavidin-488 complex being found in the nucleus by confocal microscopy of the treated cells;
- 4) SEQ ID NOS: 2-5 facilitate the internalization and nuclear localization of protein complexes as well as intact M13 phage;
- 5) SEQ ID NOS: 1-6 have been synthesized and biotinylated;
- 6) SEQ ID NOS: 1-6 facilitate peptide-B-gal complex internalization into Hig-82 cells;
- 7) SEQ ID NOS: 2-5 are more effective than the commercially available antennapedia peptide;

8) SEQ ID NOS: 3 and 5 facilitate the internalization of B-gal into murine tumor cells *in vivo*.

According to page 18, lines 11-20 of the specification, "the internalizing peptides of the present invention may be identified by fusion of an internalizing peptide of the present invention with another peptide with a desired function such as . . . fusion of an internalizing peptide to a previously identified ubiquitin targeting peptide which **may** have the amino acid sequence . . . set forth by SEQ ID NO: 73 or fusion of an internalizing peptide with an endoplasmic reticulum (ER) localization signal such as adenovirus E19 sequence which **may** have the amino acid sequence . . . as set forth by SEQ ID NO:74. In addition, the internalizing peptide of the present invention **may** have the amino acid sequence . . . (SEQ ID NO:75)". SEQ ID NOS: 73-75 are not enabling because the exact function of these peptides are not known; the identity of these peptides are speculative.

In addition, according to page 23, lines 3-9 of the specification, SEQ ID NO:69 is homologous to a bacterial protein, SEQ ID NO: 71 is homologous to a yeast **hypothetical** protein, and SEQ ID NO: 72 is homologous to herpesvirus 1 "**probably** nuclear antigen protein." Finally, there are no working examples or any mention in the specification of the properties of SEQ ID NOS: 7-18, 25-68, and 70. According to Skolnick and Fetrow (TIBTECH Jan. 2000, Vol. 18, pages 34-39), "Sequence-based methods for function prediction are inadequate because of the multifunctional nature of proteins. However, just knowing the structure of the protein is also insufficient for

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prediction of multiple functional sites" (see abstract, Box 1, and Box 2). Although the peptides of SEQ ID NOS: 69 and 71-75 are identified in the specification, it is not possible to speculate the function or utility of these peptides.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to:

- (1) the breadth of the claims;
- (2) the nature of the invention;
- (3) the state of the prior art;
- (4) the level of one of ordinary skill;
- (5) the level of predictability in the art;
- (6) the amount of direction provided by the inventor;
- (7) the existence of working examples; and
- (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

See *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

(1-2) The breadth of the claims and the nature of the invention: The claims are drawn to a peptide that facilitates cellular internalization of a cargo and provides for nuclear translocation in a target cell. The claimed invention explicitly describes the use of six peptides (SEQ ID NOS: 1-6) to facilitate cellular internalization of cargo and provide for nuclear translocation, yet includes over 60 other peptides in the specification. Since the



specification only discusses the utility of SEQ ID NOS: 1-6, the claimed invention is of a general nature.

(3 and 5) The state of the prior art and the level or predictability in the art: Due to the general nature of the invention, there are many variables to consider before using the disclosed invention. There are many methods of creating peptides and peptide fragments, in addition to the many different experiments disclosed in the specification to prove that the peptides can facilitate cellular internalization of cargo and nuclear translocation. While the claimed invention discusses and gives examples of cellular internalization for SEQ ID NOS: 1-6, there are no examples using the remainder of the peptides. The specification is silent regarding peptides of SEQ ID NOS: 7-18, 25-68, and 70 and does not show utility of SEQ ID NOS: 69 and 71-75. In the absence of sufficient teachings in the specification, one of ordinary skill in the art would require undue experimentation to prove that all the claimed peptides other SEQ ID NOS: 1-6 facilitate cellular internalization of cargo and provide nuclear translocation.

(4 and 8) The level of one of ordinary skill and the quantity of experimentation needed to make or use the invention based on the content of the disclosure: The level of skill would be high, most likely at the Ph.D. level or one with skills in peptide synthesis, histology, and eukaryotic cellular biology. However, the instant disclosure is based on six peptides (SEQ ID NOS: 1-6) that facilitate cellular internalization of cargo and nuclear translocation and nowhere in the specification guidance is given as to the other

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peptides. From the specification of the disclosure, one skilled in the art would determine the properties of all the peptides; they would have to engage in undue (non-routine) experimentation to carry out the invention as claimed. Due to the lack of evidence that the peptides other than SEQ ID NOS: 1-6 facilitate cellular internalization of cargo and provide nuclear translocation, one skilled in the art would have to use a trial and error method to practice the claimed invention. Note that there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and use the invention as broadly as it is claimed. Therefore, it is deemed that further research of an unpredictable nature would be necessary to make or use the invention as claimed. Thus, due to the inadequacies of the instant disclosure, one of ordinary skill would not have a reasonable expectation of success and the practice of the full scope of the invention would require undue experimentation.

(6-7) The amount of direction provided by the inventor and the existence of working examples: Applicants have only provided six peptides that facilitate cellular internalization of cargo and nuclear translocation and do not give examples using the other 75 peptides. In addition, the instant specification does not discuss the utility of the other 75 peptides. As a result, the instant invention is claiming peptides that do not have disclosed utility. The claimed invention is very broad and does not give adequate direction to one skilled in the art to utilize the claimed invention as stated.

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15. **Claims 1, 2, and 7** are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

To satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The present claims are directed to peptides that facilitate cellular internalization of cargo and provides for nuclear translocation. However, the specification has evidence that only peptides of SEQ ID NOS: 1-6 facilitate cellular internalization of cargo and provide for nuclear translocation. In addition, the specification fails to describe the properties of the peptides of SEQ ID NOS: 7-18, 25-68, and 70. Finally, there is speculation as to the homology of the peptides of SEQ ID NOS: 69 and 71-75 to known peptides. Since the peptides of SEQ ID NOS: 69 and 71-75 *may* be homologous to known peptides, it is not possible to predict the function of these peptides.

With regard to the description requirement, Applicants' attention is directed to The Court of Appeals for the Federal Circuit which held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1405 (1997), quoting *Fiers v. Revel*, 25 USPQ2d

1601, 1606 (Fed. Cir. 1993) (bracketed material in original)[The claims at issue in *University of California v. Eli Lilly* defined the invention by function of the claimed DNA (encoding insulin)].

Although directed to DNA compounds, this holding would be deemed to be applicable to any compound; which requires a representative sample of compounds and/or a showing of sufficient identifying characteristics, to demonstrate possession of the claimed generic(s).

In the present instance, the claimed invention contains no identifying characteristics regarding peptides other than those of SEQ ID NOS: 1-6. There is a lack of working examples for the other sequences disclosed in the specification. Since the sequences are not known in the prior art, a person skilled in the art will have to partake in undue experimentation to predict the function and properties of the unknown peptides.

### **Conclusion**

16. No claims are allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Steven Tizio whose telephone number is (703) 305-1903. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jyothsna Venkat, can be reached at (703) 308-2439. The fax phone number for the organization where this application or proceeding is assigned is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

  
**PADMASHRI PONNALURI**  
**PRIMARY EXAMINER**

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